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RAPID HYDROLYSIS AND ABSORPTION OF STRUCTURED MEDIUM-CHAIN TRIGLYCERIDES

The structured lipid 1,3-dioctanoyl-2-linoleoyl glycerol was more rapidly hydrolyzed and absorbed than triglycerides containing all long-chain fatty acids.

Key Words: lipolysis, medium-chain triglycerides, long-chain triglycerides, structured triglycerides, malabsorption, pancreatic insufficiency, total parenteral nutrition

Medium-chain triglycerides (MCT) of octanoic (8:0 or caprylic) and decanoic (10:0 or capric) acids are beneficial in the treatment of patients with the malabsorption syndrome.[1,2] In the mouth, MCT provide the feel and taste of fats and are a dense form of calories, compared with carbohydrates.[2] The acids in MCT do not require the formation of chylomicrons, are absorbed via the portal system, are not carnitine-dependent, are readily oxidized, and do not deposit in adipose tissue. They do not, however, generally provide essential fatty acids (EFA). In conditions utilizing MCT administration, such as cystic fibrosis, a highly polyunsaturated vegetable oil is added to provide EFA. In contrast, lipid emulsions given as a part of total parenteral nutrition (TPN) contain soybean or safflower oils that contain long-chain triglycerides (LCT), mostly of oleic acid (18:1 *n*-9) and linoleic acid (18:2 *n*-6). The LCT, however, are slow to clear from the blood, oxidize slowly, and tend to deposit in fat cells.

The optimum lipid structure for parenteral use would thus appear to be structured triglycerides, that is, having both medium-chain and polyunsaturated fatty acids on the same glycerol molecule. A struc-

tured lipid containing about 25 percent 18:2 appears to be optimal for TPN.[1] There have been several studies on the use of structured lipids in animals and humans,[1-9] particularly for the treatment of patients with cystic fibrosis and pancreatic insufficiency.[3] The structured lipids provided EFA and energy to cystic fibrosis patients. In *some cases, however, the structured lipids* were simply physical mixtures of 75 percent MCT and 25 percent LCT. True structured lipids are made by rearrangement of trioctanoin with 18:2 to produce mixtures of triglycerides containing 8:0 and 18:2. This has been accomplished by Jandacek et al,[10] who investigated the hydrolysis and absorption of triglycerides with octanoic acid in the 1 and 3 positions and a long-chain fatty acid in the 2 position.

The 1,3-dioctanoyl and 1,3-diacetyl triglycerides and those synthesized from [1-^{14}C]linoleoyl chloride were purified as described by Mattson and Volpenhein.[11] The other oils were purchased from appropriate sources. Structural integrity of the synthesized triglycerides was determined by digestion with pancreatic lipase and separation and identification by gas-liquid chromatography of the resulting 2-monoglycerides and free fatty acids.[12]

Initial screening of in vitro hydrolysis rates of six fats of various chain lengths and triglyceride structure was done with fresh rat bile and pancreatic fluid. The fats were vigorously stirred in buffer with the mixture kept at pH 8.9 to 9.0 by addition of 0.1 N KOH monitored by a pH electrode. Rates of hydrolysis of 2-linoleoyl-1,3-dioctanoyl glycerol (8:0-18:2-8:0), sunflower oil, and the four Captex 810 series of preparations were similarly compared, except that a porcine pancreatic lipase preparation (steapsin) and a pH stat system was used to measure the release of fatty acids. The Captex triglycerides varied in their linoleate content from 10 to 45 percent and reciprocally in their octanoate/decanoate content from 80 to 32 percent. Captex A had the least linoleate content and D had the largest. The rate of fatty acid released per minute was taken from the linear portion of the plot of added base vs time during the first 1 to 4 minutes of the reaction. Isolated, irrigated loops of rat small intestine were injected with 2-[1-^{14}C]linoleoyl-1,3-dioctanoyl glycerol (8:0-18:2*-8:0) or 18:1-18:2*-18:1. After 45 minutes the animals were sacrificed, the loop contents extracted, the products of lipolysis separated by thin-layer chromatography, and their quantities assayed by scintillation counting.

The relative rates of hydrolysis of substrates of various chain length and structure by rat pancreatic lipase were 8:0-18:1-8:0 = 7:0-7:0-7:0 > 10:0-10:0-10:0 > 2:0-18:1-2:0 > 2:0-2:0-2:0. The rates for the steapsin-catalyzed hydrolysis as a function of mass were MCT > 8:0-18:2-8:0 > sunflower oil. When triglycerides of random structure containing various long- and medium-chain fatty acids (Captex 810 series) were hydrolyzed with steapsin, the relative rates were Captex A > B > C = D. The amounts of 18:2 increased and of 8:0 + 10:0 decreased as the rates of lipolysis declined. Within each of these trials the rate of hydrolysis of each fat differed significantly ($p < 0.05$) from that of each of the other fats with two exceptions: MCT and 8:0-18:2-8:0 did not differ, nor did Captex 810 C and D.

Significantly more 8:0-18:2*-8:0 than 18:1-18:2*-18:1 was hydrolyzed and absorbed in the isolated loop studies. Absorption of 8:0-18:2*-8:0 was 44.9 percent and for 18:1-18:2*-18:1 it was 16.4 percent. The amount of unhydrolyzed 8:0-18:2*-8:0 was 11.1 percent and for 18:1-18:2*-18:1 it was 48.3 percent.

The structured triglyceride 8:0-18:2-8:0 was hydrolyzed and absorbed more rapidly than LCT. This type of fat combines the best features of MCT and LCT lipids in the treatment of pancreatic insufficiency. With 8:0-18:2-8:0, the octanoic acids are rapidly hydrolyzed and absorbed. The EFA requirement is met by the easily absorbed 2-monoglyceride of 18:2. The nonstructured Captex mixtures, similar to 8:0-18:2-8:0, were hydrolyzed about 40 percent less rapidly than the structured triglyceride.

Based on the results provided by Janda-

cek et al,[10] 8:0-18:2-8:0 should be useful in cases of pancreatic insufficiency. The need for more investigation is obvious, but it will likely be limited by the availability of particular structured triglycerides. Although laboratory synthesis of 8:0-18:2-8:0 is not difficult, purification can be arduous, and quantities are limited to about 100 g. Pilot plant output of these interesting lipids should provide sufficient quantities for further clinical investigation.

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TRANSPORT PROPERTIES OF FOLATE BOUND TO HUMAN MILK FOLATE-BINDING PROTEIN

Folate bound to human milk folate-binding protein is absorbed in the jejunum by the same carrier as folate, but more slowly. This may improve the nutritional bioavailability of folate.

Key Words: folate, intestinal transport, human milk, binding protein

Since the discovery of folate-binding protein (FBP) in milk by Ghitis[1] in 1966, its physiologic role has been a subject of investigation and speculation. Two functions have been suggested: 1) concentration of folate in the mammary gland,[2] and 2) protection of folate from its utilization by folate-dependent intestinal bacteria.[3,4] The former is based on the property of tight binding of folate to the milk-binding protein, and the latter is based on the observation that the uptake of bound folic acid (PteGlu) by folate-dependent intestinal